Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application. Please amend claims 80 and 85.

Listing of Claims:

1. - 79. (Canceled)

80. (Currently Amended) A ligand-activated uni-molecular detector comprising:

a circularly permutated marker protein comprising a first interactor domain covalently bonded to the circularly permutated marker protein through an N-terminal breakpoint of the circularly permutated marker protein and a second interactor domain covalently bonded to the circularly permutated marker protein through a C-terminal breakpoint **of the** circularly permutated **[[of the]]** marker protein, wherein said circularly permutated marker protein is functionally reconstituted only upon binding of said first interactor domain and said second interactor domain to a single ligand.

81. (Previously Presented) The ligand-activated uni-molecular detector of claim 80, wherein said circularly permutated marker protein is a circularly permutated enzyme.

82. (Previously Presented) The ligand-activated uni-molecular detector of claim 81, wherein said circularly permutated enzyme is a β-lactamase protein.

83. (Previously Presented) The ligand-activated uni-molecular detector of claim 82, wherein said circularly permutated enzyme is a TEM-1 β-lactamase protein.

84. (Previously Presented) The ligand-activated uni-molecular detector of claim 80, wherein said N-terminal break point and said C-terminal break point are within a solvent exposed loop between elements of secondary structure within the enzyme.

85. (Currently Amended) The ligand-activated uni-molecular detector of claim 80, wherein said circularly permutated protein [[is]] consists essentially of a β-lactamase protein with the following numbering convention:

His Pro Glu Thr Leu Val Lys Val Lys Asp Ala Glu Asp Gln Leu Gly
26 30 35 40
Ala Arg Val Gly Tyr Ile Glu Leu Asp Leu Asn Ser Gly Lys Ile Leu
45 50 55
Glu Ser Phe Arg Pro Glu Glu Arg Phe Pro Met Met Ser Thr Phe Lys
60 65 70
Val Leu Leu Cys Gly Ala Val Leu Ser Arg Ile Asp Ala Gly Gln Glu
75 80 85
Gln Leu Gly Arg Arg Ile His Tyr Ser Gln Asn Asp Leu Val Glu Tyr
90 95 100 105
Ser Pro Val Thr Glu Lys His Leu Thr Asp Gly Met Thr Val Arg Glu
110 115 120
Leu Cys Ser Ala Ala Ile Thr Met Ser Asp Asn Thr Ala Ala Asn Leu
125 130 135
Leu Leu Thr Thr Ile Gly Gly Pro Lys Glu Leu Thr Ala Phe Leu His
140 145 150
Asn Met Gly Asp His Val Thr Arg Leu Asp Arg Trp Glu Pro Glu Leu
155 160 165
Asn Glu Ala Ile Pro Asn Asp Glu Arg Asp Thr Thr Met Pro Val Ala
170 175 180 185
Met Ala Thr Thr Leu Arg Lys Leu Leu Thr Gly Glu Leu Leu Thr Leu
190 195 200
Ala Ser Arg Gln Gln Leu Ile Asp Trp Met Glu Ala Asp Lys Val Ala
205 210 215
Gly Pro Leu Leu Arg Ser Ala Leu Pro Ala Gly Trp Phe Ile Ala Asp
220 225 230

Lys Ser Gly Ala Gly Glu Arg Gly Ser Arg Gly Ile Ile Ala Ala Leu
235 240 245
Gly Pro Asp Gly Lys Pro Ser Arg Ile Val Val Ile Tyr Thr Thr Gly
250 255 260 265
Ser Gln Ala Thr Met Asp Glu Arg Asn Arg Gln Ile Ala Glu Ile Gly
270 275 280
Ala Ser Leu Ile Lys His Trp
285
(SEQ ID NO: 2);

~~comprising amino acids 1 to 263 of SEQ ID: NO 2,~~ wherein said N-terminal breakpoint and said C-terminal breakpoint are within 10 amino acids of an amide bond junction between two amino acids selected from the group consisting of asparagine 52 and serine 53, leucine 91 and glycine 92, glutamine 99 and asparagine 100, proline 174 and asparagine 175, glutamic acid 197 and leucine 198, lysine 215 and valine 216, alanine 227 and glycine 228, and glycine 253 and lysine 254.

86. (Previously Presented) The ligand-activated uni-molecular detector of claim 85, wherein said two amino acids are selected from the group consisting of proline 174 and asparagine 175, glutamic acid 197 and leucine 198, lysine 215 and valine 216, alanine 227 and glycine 228, and glycine 253 and lysine 254.

87. (Previously Presented) The ligand-activated uni-molecular detector of claim 85, wherein said two amino acids are glutamic acid 197 and leucine 198.

88. (Previously Presented) The ligand-activated uni-molecular detector of claim 80, wherein said ligand is a protein ligand.

89. (Previously Presented) A method of detecting the presence of a target ligand using a ligand-activated uni-molecular detector comprising the steps of:

(a) contacting said target ligand with said ligand-activated uni-molecular detector, said ligand-activated uni-molecular detector comprising a circularly permutated marker protein comprising a first interactor domain covalently bonded to the circularly permutated marker protein through an N-terminal breakpoint of the circularly permutated marker protein and a second interactor domain covalently bonded to the circularly permutated marker protein through a C-terminal breakpoint of the circularly permutated marker protein;

(b) allowing said target ligand to bind to said first interactor domain and said second interactor domain;

(c) after step (b), allowing said circularly permutated marker protein to functionally reconstitute;

(d) detecting the functionally reconstituted circularly permutated marker protein thereby detecting the presence of said target ligand.